Sex ratios of births, mortality, and air pollution: can measuring the sex ratios of births help to identify health hazards from air pollution in industrial environments?

F L R Williams, S A Ogston, O L Lloyd

Abstract

Objectives—To compare the sex ratios of births and mortality in 12 Scottish localities with residential exposure to pollution from a variety of industrial sources with those in 12 nearby and comparable localities without such exposure. Methods—24 localities were defined by postcode sectors. SMRs for lung cancer and for all causes of death and sex ratios of births were calculated for each locality for the years 1979–83. Log linear regression was used to assess the relation between exposure, sex ratios, and mortality.

Results—Mortalities from all causes were consistently and significantly higher in the residential areas exposed to air pollution than in the non-exposed areas. A similar, but less consistently significant, excess of mortality from lung cancer in the exposed areas was also found. The associations between exposure to the general air pollution and abnormal sex ratios, and between abnormal sex ratios and mortality, were negligible.

Conclusions—Sex ratios were not consistently affected when the concentrations or components of the air pollution were insufficiently toxic to cause substantially increased death rates. Monitoring of the sex ratio does not provide a reliable screening measure for detecting cryptic health hazards from industrial air pollution in the general residential environment.

Keywords: sex ratios; mortality; residential exposure; industrial pollution

Abnormal sex ratios* of births (100 males ÷ females) have been clearly associated with specific occupational environments. These associations have suggested that parental exposure to some occupational pollutants may be a determinant of the sex ratio of their offspring. If exposure to pollutants within industries can cause an imbalance of the sex ratio in the workers' offspring, it is conceivable that air pollution from those industries might also cause abnormal sex ratios in the offspring of residents of the neighbourhoods exposed to those pollutants. Sex ratios have been studied in considerable detail but few studies could be found in which possible associations were investigated between sex ratios and air pollution of the general environment. In five retrospective studies, abnormal sex ratios were found in residential areas exposed to air pollution. The pollution reported in three of the studies had been readily seen and smelt, and had also been associated with significant excess mortality in the exposed populations (possibly because of the quantity or quality of its toxicity). The pollution in the fourth study had also been visible and was often highly acrid, and had been associated strongly with animal mortality and morbidity and with high frequencies of twin births in animals and in humans. The fifth study did not include any estimate of mortality or morbidity.

The mechanism of how pollution could affect the sex ratios of births is not clear, but the metabolism of the rapidly dividing cells of the gonadal and fetal tissues is likely to be particularly vulnerable to the influences of pollutants. The association between the nematocide DBCP (1,2-dibromo-3-chloropropane) and low sex ratios, for example, was thought to be consistent with the spermatozoa that bear the Y chromosome being damaged by exposure to DBCP, because both exposed and non-exposed workers had similar proportions of spermatozoa bearing the Y chromosome.

The question remained of whether this association between air pollution, sex ratios, and mortality also existed in localities where the pollution was from a broad range of industrial sources and probably in lower concentrations or of a less specific nature. If so, the detection of such abnormalities in the sex ratio would constitute a simple screening procedure for alerting medical and environmental health authorities to the presence of cryptic hazards to health from general industrial air pollution. This study, therefore, was designed to explore two hypotheses. Firstly, that the sex ratio of births would be altered, to either high or low, where the parents have been exposed to environmental air pollution from a range of industries. Secondly, that the mortality from lung cancer or from all causes of death would be higher in those exposed areas.

*(In this paper, the term "sex ratio" is used in place of the correct but longer term "secondary sex ratio" to refer to liveborn children only.)
**Methods**

Twenty-four localities in Scotland were identified. The basic units of the study were defined by the postcode sectors of the national system of postcode registration. Postcodes in Scotland operate at four levels: area, district, sector, and unit, of which there are 15, 416, 898, and 124634 respectively. Postcode units, although differing in size geographically, are delineated to represent roughly equal population sizes. The localities consisted of 12 exposed localities matched to 12 non-exposed localities, categorised according to predetermined criteria (table 1). No networks of air sampling stations for monitoring objectively the quality and quantity of air pollution in the localities were in existence, nor had any been in the past. As is customary in these circumstances we used an indirect approach to the assessment of the probable category of exposure—that is, exposed or non-exposed—to which each location should be assigned. This was the approach we had used successfully in a previous study, and it was derived from our experience in earlier studies in which air pollution samplers had been used and which had indicated the importance of local topographies and the directional axes linking pollution sources to populations.

Because we were evaluating the sex ratio as a measure of screening for the biological effects of generalised industrial air pollution, a variety of sources of industrial pollution were included in the study (table 2). To assess the consequences of exposure to a heterogeneous range of sources of pollution on the sex ratio was a novel part of the design of the study, which we had specifically chosen to differentiate from our previously published work on single and specific industrial sources. Different pollutants affect the sex ratio in different ways and may cause both abnormally high and abnormally low sex ratios. To accommodate this, all of the exposed localities selected were exposed either to a single source of pollutant or, where this was not possible, to similar types of industrial pollution from a compact source of exposure.

Each locality comprised a few postcode sectors (range 1–7). For each postcode sector (the data unit of the study), data on births, deaths, the percentage of men in employment, and the percentage of residents born in the United Kingdom were obtained from the General Register Office in Edinburgh. Scottish rates of mortality, derived from contemporaneous annual reports of the Registrar General, were used as standards for the calculation of standardised mortality ratios (SMRs).

Results were analysed at two levels: the 12 exposed and 12 non-exposed localities and also for the individual postcode sectors that made up those localities.

**ANALYSIS OF INDIVIDUAL POSTCODE SECTORS**

There were 72 postcode sectors in the data set of which 35 were in exposed localities and 37 were in non-exposed localities. Sex ratios were calculated for all of the sectors for the years 1979–83. The significance of the sex ratios in each sector was determined with the normal approximation to the binomial distribution by calculating the \( Z \) statistic:

\[
Z = (x - NP) \div \sqrt{NPQ}
\]

where: \( x \) = number of boys; \( N \) = total number of boys and girls; \( P \) = the Scottish proportion of boys (106 = 206); \( Q \) = the proportion of girls (1 - P).

When \( Z \geq 1.96 \), \( P < 0.05 \)

The SMRs and their 95% confidence intervals (95% CIs) for lung cancer and for all causes of death were calculated for each of the exposed and non-exposed postcode sectors for the years 1979–83. These years were selected to afford stability and thus confidence in the population values used in calculation of the SMRs.

**LOG LINEAR MODELLING WITH THE SECTOR DATA**

Log linear modelling (GLIM) was used to analyse the mortality and sex ratio data at the sector level. This method aims to express log SMR as a linear function of explanatory variables. The variables in the model were exposure (0 = no exposure, 1 = exposure), log sex ratio, and percentage of men in employment. As data on smoking habit were
Table 3: Summary of the log linear regression of all causes of death and lung cancer deaths with GLIM

<table>
<thead>
<tr>
<th>Variable</th>
<th>Death rate Estimate</th>
<th>SEM (corrected)</th>
<th>Relative risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lynch cancer 0-1708</td>
<td>0-0462</td>
<td>1-18 (1-08 to 1-30)</td>
<td></td>
</tr>
<tr>
<td>All causes 0-1758</td>
<td>0-0117</td>
<td>1-19 (1-16 to 1-22)</td>
<td></td>
</tr>
</tbody>
</table>

Adjustment for sex and employment

Model 1:

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Death rate Estimate</th>
<th>SEM (corrected)</th>
<th>Relative risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lynch cancer 0-0558</td>
<td>0-0668</td>
<td>1-06 (0-93 to 1-21)</td>
<td></td>
</tr>
<tr>
<td>Employment</td>
<td>-0-0181</td>
<td>0-0065</td>
<td>0-93 (0-83 to 0-95)</td>
</tr>
<tr>
<td>G*</td>
<td>141-9</td>
<td>68</td>
<td></td>
</tr>
</tbody>
</table>

Model 2:

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Death rate Estimate</th>
<th>SEM (corrected)</th>
<th>Relative risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lynch cancer 0-0537</td>
<td>0-0658</td>
<td>1-06 (0-93 to 1-20)</td>
<td></td>
</tr>
<tr>
<td>Employment</td>
<td>-0-0179</td>
<td>0-0066</td>
<td>0-98 (0-97 to 1-00)</td>
</tr>
<tr>
<td>G*</td>
<td>141-5</td>
<td>68</td>
<td></td>
</tr>
</tbody>
</table>

unobtainable, percentage of men in employment, which reflects social class, was used instead of smoking levels.) We used two models:

Model 1: log SMR = α + β1(exposure) + β2(log SR) + β3(men in employment).

Model 2: log SMR = α + β1(exposure) + β2(log SR) + β3(men in employment).

The model first tested a high sex ratio indicated a high mortality and the second model tested for whether an extreme sex ratio (either high or low) indicated high mortality. The model that included (log SR)2 was probably more appropriate than that which included (log SR), as exposure was coded 1 for exposed and 0 for non-exposed, β represented the difference in the log SMR between the exposed and non-exposed localities. The antilog of β gave the relative risk for exposure adjusted for the other variables in the model. Thus, the equation described the effect of exposure on the SMR. The GLIM system reports the parameter estimates for α and β with their SEMs and tests of significance. Two SEMs were calculated. The first SEM was based on a Poisson assumption obtained from GLIM, the second SEM was corrected and allowed for the variability outside the Poisson assumption as shown by the magnitude of the difference between the goodness of fit statistic (G2) and its degree of freedom (= 68). We report in this paper only the corrected SEM.

For comparison, we also computed the logistic regression of sex ratio on exposure and percentage of men employed.

LOCALITY ANALYSIS

The sector data were subsumed to make 12 exposed matched to 12 non-exposed localities. For the years 1979–83, the sex ratios and SMRs for lung cancer and for all causes of death were calculated for each of the exposed and non-exposed localities and the results were compared.

For each of the 12 matched localities, the SMR and sex ratio were calculated for the exposed (denoted as ex) and non-exposed exposed (denoted as ne) localities. The overall association was graphically represented by plotting Y against X where

Y = SMRe - SMRne and X = SRex - SRne

The study was planned with 12 exposed and 12 non-exposed localities, with 40 expected deaths in each. The significance was evaluated by a regression of Y = SMRex - SMRne against X = SRex - SRne. The total sample was sufficient to detect a difference in Y of 0-6, with a power of 85%.

Results

SECTOR ANALYSIS

According to the data in the 1981 census, the numbers and percentages of people born in the United Kingdom exposed and non-exposed sectors did not differ appreciably (P > 0.05). Overall, the mean percentages born in the exposed and non-exposed sectors respectively were 96%-6% and 95.7%.

LOG LINEAR MODELLING

Regression of log SMR on exposure alone showed that mortality for lung cancer and for total mortality was significantly higher in the exposed than in the non-exposed localities (table 3).

Table 3 shows the regression coefficients and SEMs for the regression of log SMR for lung cancer and for all causes of mortality on (log SR), (log SR)2, % employment, and
exposure. The SMRs for mortality from all causes in the exposed localities were significantly higher than those in the non-exposed localities (relative risk 1·12, 95% CI 1·06-1·18). The difference between the SMRs for lung cancer in the exposed and non-exposed localities was reduced to a non-significant relative risk (1·06, 95% CI 0·93-1·21). For all causes of death, the addition of \((\log SR)^2\) in the model maintained the significant association between total mortality and exposure (relative risk 1·12, 95% CI 1·05-1·18). Lung cancer mortality showed a positive association with \((\log SR)^2\) and exposure, but all causes mortality showed a negative association with \((\log SR)\).

The regression of the sex ratio on exposure and employment was not significant (odds ratio 1·03, 95% CI 0·98-1·07). This mirrored the results of the locality analysis.

**Locality Analysis**

The sex ratios were higher in the exposed localities in only seven of the 12 matched localities; however, none of these differences was significant (table 4). For lung cancer, nine of the 12 exposed localities had SMRs higher than the SMRs in their equivalent non-exposed localities, but for only one of these nine was the difference significant (table 4). For all causes of death, by contrast, 10 of the exposed localities had higher SMRs than the non-exposed localities, nine of these differences were significant, and in only one area was the SMR for the exposed locality significantly lower than its counterpart (table 4).

The scatter plot (fig 1) of the relation between the difference in the SMR for lung cancer for the exposed and non-exposed localities (SMR exposed - SMR non-exposed) on the y axis and the difference between the sex ratios for the exposed and non-exposed localities (SR - SRne) on the x axis, showed only a weak association (rho = 0·224). Only three localities showed extreme differences. Between all causes of death and the sex ratio (fig 2), the relation was slightly stronger (rho = 0·306).

Because the distributions of the SMRs and sex ratios among the localities were consistent with normal distributions, the overall means for the sex ratios and SMRs were compared with the Student’s \(t\) test. The means of the sex ratios did not differ significantly between the exposed and non-exposed localities (table 5). The mean SMRs for the exposed localities were significantly higher both for lung cancer and for all causes of death than the corresponding SMRs for the non-exposed localities (table 5).

**Discussion**

The United Kingdom’s Clean Air Acts of the 1950s and 1960s have successfully reduced the gross health hazards caused by particulate matter and sulphurous compounds. The environmental air pollution, of increasing importance to public health in the 1970s and beyond, includes the less visible pollutants that contain the heavy metals and organic compounds (table 2). Perinatal and infant mortality were once crucial variables by which the quality of the public’s health was measured; with improved general health and access to medical care, however, these variables have become less discriminating. It has been suggested that as the sex ratio of births might be considered to reflect deaths at much earlier stages, this variable might be used to monitor the quality of public health.

Obstetric epidemiology would have the advantage over other variables of chronic disease of a relatively short latency between exposure and measurable outcome.

Previous studies showed that the sex ratio of births could be abnormal where pollution concentrations from specific industrial processes were sufficiently toxic to cause clear cut increases in the contemporaneous rates for all causes of death and in particular for lung cancer. As one of the aspirations of environmental epidemiology is to identify hazardous environments before they cause

**Table 5** The overall means of the sex ratios and of the SMRs for lung cancer and all causes in the localities exposed and non-exposed to industrial pollution.

<table>
<thead>
<tr>
<th>Sex ratio:</th>
<th>Mean (SD)</th>
<th>t Statistic</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposed</td>
<td>107 (9)</td>
<td>0.436</td>
<td>0.672</td>
</tr>
<tr>
<td>Non-exposed</td>
<td>105 (8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SMRs lung cancer:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exposed</td>
<td>113 (38)</td>
<td>2.461</td>
<td>0.032</td>
</tr>
<tr>
<td>Non-exposed</td>
<td>88 (15)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SMRs all causes:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exposed</td>
<td>103 (8)</td>
<td>3.68</td>
<td>0.004</td>
</tr>
<tr>
<td>Non-exposed</td>
<td>90 (6)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
gross morbidity or mortality, a study was needed in which communities exposed to
less obvious pollution from a wider range of sources were examined. In our study,
however, no convincing evidence was found that exposure to generalised airborne pollution was associated with abnormal sex ratios, and a non-significant negative relation was present between abnormal sex ratios and total mortality.

The SMRs in the exposed localities were significantly higher than those in the non-exposed localities for total mortality and (less consistently) for lung cancer. The non-exposed localities had been selected because of their geographical proximity to, and environmental comparability with, the exposed localities. Hence, an allowance for socioeconomic variables in the study units was intrinsic in the comparisons. After the SMRs had been adjusted further by taking into account the percentage of men in employment (used instead of social class and hence for smoking) the difference between the SMRs for lung cancer of the exposed and the non-exposed localities was no longer significant, although that difference did remain significant for all causes of death. Because of the known relation between lower social classes and both higher consumption of tobacco and higher mortality, we decided to introduce this variable and treat it as a potential confounding factor.

These observations showed two methodological difficulties frequently encountered in environmental epidemiology. The first difficulty was how to control adequately for differences of general socioeconomic factors without risking overcontrol. Our first method of matching the two types of locality for general environmental circumstances and social class (and hence smoking), by geographical proximity, ethnicity, and general perception of the localities, had credibility in being derived from a direct assessment of the study areas themselves, but was partly subjective. With this method, the close comparability of the values of ethnicity between exposed and non-exposed populations supported the view that the socioeconomic structures of the two types of locality might be similar. Our additional method, incorporating the percentage of men in employment instead of social class, was based totally on an objective variable and was valid on a national basis. We had no evidence, however, that this indirect measure of smoking accurately reflected any differences of social class (and smoking habits) between the neighbouring localities in this particular study.

It is always conceivable that occupational exposures (for which data are not available) could play a part in environmental patterns of disease and sex ratios of births. The distances from the pollution sources of most of the non-exposed localities were comparable to those from the exposed localities. Indeed the comparison localities had been chosen because they satisfied that condition. In a previous study in which this question was pursued exhaustively, there was no confounding of the pattern through occupational experience.25

How best to estimate the flow of air pollution in the nearby localities and hence their assignment into exposed and non-exposed categories is the second methodological difficulty. It is often met in environmental epidemiological studies where (usually) no comprehensive network of sites exists for monitoring the spread of air pollution from defined industrial sources. In studies of similar relations, conventionally only the proximity between the addresses of cases and the sources of pollution has been used.23 In addition to this measure, we also took into account the important influences of wind direction, topography, and height of the sources of pollution on the probable distribution of the pollution. Nevertheless, this method ultimately and inevitably lacks precision because the exposed and the not exposed localities (if nearby) cannot be accurately demarcated in the absence of measurements of chemical concentrations in environmental samples. The cause-effect relation is likely to be artefactually weakened in the exposed localities and strengthened in the non-exposed localities.

In our study, the assessment did not include information about the total exposure of the parents to the pollution, and so some births might have been misclassified with regard to antenatal exposure. Uncertainties on this point exist for both the at risk exposed areas and the non-exposed comparison areas, and there is no reason to suppose that one differed appreciably from the other. Lastly, other factors that can affect the sex ratio (such as parental age, parity, and exposure to disease) were unavailable and therefore could not be taken into account. In view of all these circumstances, therefore, any impact of the pollution upon the sex ratios (and mortality) that was found in this study must have been artefactually low. Nevertheless, despite the inherent imprecision of the exposure categories, differences in mortality between the exposed and non-exposed types of locality remained, with the mortality from all causes remaining significantly high with all the analytical tests.

The tests for the two hypotheses of this study led to two conclusions with their related implications. Firstly, the sex ratios of births were not consistently affected in areas where the toxicity of the pollution was either of the wrong chemical composition to produce that effect or was insufficient to cause large and unequivocally significant increases in the SMRs from both total mortality and lung cancer. Therefore, the routine monitoring of sex ratios of births is unreliable as a screening measure for the detection of cryptic health hazards in general industrial environments. Hence, the search for further specific types of pollution that affect the sex ratios of births should be pursued. Secondly, the areas exposed to pollution from a range of industrial sources had higher SMRs for lung
Sex ratios of births, mortality, and air pollution

cancer and particularly for all causes of mortality than the unexposed areas, even when the definition of exposure was based on estimates rather than on data from a sampling network for air pollution. This finding indicated the need for investigations to exclude the possible effects of other confounding variables and to determine the sources of the toxic air pollutants those environments. It also suggested that public health authorities could monitor the mortality in their populations exposed to industrial pollution even in the absence of detailed information from pollution monitoring networks. If one cause-effect relation suggested in this paper is confirmed by such studies, the findings would also indicate that the legislation on air quality control should be strengthened to minimise exposures to these environmental hazards.

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6 Jakobovits AA. Sex ratio of spontaneously aborted fetuses should be not more than 500 words in length and contain a minimum of references. Tables and figures should be kept to an absolute minimum. Letters are accepted on the understanding that they may be subject to editorial revision and shortening.

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8 Williams FLR, Lawson AB, Lloyd OL. Low sex ratios of births in areas at risk from air pollution from incinerators, as shown by geographical analysis and 3-dimensional mapping. Int J Epidemiol 1992;21:311-9.
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